Borane-Catalyzed Heterocycle Synthesis

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ORIGIN

Over the past few years, main group reagents (particularly Lewis acidic boranes) have garnered significant attention in synthetic bond-forming processes. Recently, tris (pentafluorophenyl)borane has been shown to activate C–C π-bonds, enabling synthesis of biologically active heterocyclic and aromatic compounds.

REACTION MECHANISM

The synthesis of heterocyclic and aromatic compounds can be achieved through borane-catalyzed activation of C–C π-bonds towards pendant nucleophiles. Recently, tris (pentafluorophenyl)borane [$B(C_6F_5)_3$] has been shown to exhibit unique properties, acting as either a hard Lewis acid with high oxophilic character or as a π-acid (analogous to gold) to activate alkynes. At the beginning of the catalytic cycle, free $B(C_6F_5)_3$ (I) is in equilibrium with the borane-carboxyl adduct (II). This was corroborated by the detection of a broad resonance in the ^{11}B NMR spectrum corresponding to the formation of this adduct. However, at an elevated temperature (70^{o}C), decomplexation of $B(C_6F_5)_3$ from the carboxyl group occurs, followed by coordination to alkyne π-bond. This coordination facilitates a 6-endo-dig cyclization (formally a trans-1,2-oxyboration) furnishing (III). Formation of (III) was determined by the observation of a transient sharp singlet at approximately −15 ppm in the ^{11}B NMR spectrum characteristic of the formation of an alkenyl borate that can be isolated when R^1 = Me. Subsequent elimination of either a carbenium ion or proton $[R^1]^+$ from the ester, followed by proto- or carbo-deboronation, yields the desired 3,4-dihydropyrone (IV) and releases $B(C_6F_5)_3$ to re-enter the catalytic cycle. While this transformation has been demonstrated for the synthesis of dihydropyrones and isocoumarins, the overall 1,2-oxoboration process is more general. As a result, a wide range of different heterocycles can be accessed in a facile manner, such as pyryliums, oxazoles, oxazolines, indoles, and dihydroquinolines, among others. All carbon scaffolds, such as polycyclic dibenzapentalenes, can also be accessed from a $B(C_6F_5)_3$-induced cyclization of 1,2-bis(phenylethynyl)benzenes.

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IMPORTANCE

The use of a strong boron-based Lewis acid to promote catalytic cyclizations is a powerful metal-free approach leading to the formation of useful heteroaromatics and aromatics. This mechanism highlights the unique behavior of $B(C_6F_5)_3$ to act as both a hard Lewis acid and π-acid, and that divergent reactivity is possible employing $B(C_6F_5)_3$ as a catalyst. Borane-catalyzed reactions allow for the synthesis of high-value products in a sustainable manner, from cheap and readily available starting materials.

Literature

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